

Evolving Technology

Effectiveness of the Cobra aortic catheter for dual-temperature management during adult cardiac surgery

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Objectives: In animals the Cardeon Cobra catheter (Cardeon Corp, Cupertino, Calif) allows independent control of aortic arch and descending aortic temperatures and profoundly reduces cerebral embolization during bypass. This investigation describes the first clinical use of the device during adult cardiac surgery. The purpose of the study was to confirm that the Cobra catheter delivers adequate cerebral and systemic perfusion while providing simultaneous cerebral hypothermia and systemic normothermia during cardiopulmonary bypass.

Methods: In a prospective multicenter study the Cobra aortic catheter was placed in 20 adults undergoing cardiopulmonary bypass. Arch and corporeal temperatures, bypass flows, and arterial blood pressures were recorded intraoperatively. Jugular bulb and mixed venous oxygen saturation was used to assess the adequacy of cerebral and systemic perfusion.

Results: Surgeons at 3 institutions placed the Cobra catheter in patients undergoing coronary artery bypass grafting ($n = 13$), valve ($n = 3$), and combined valve-bypass ($n = 4$) operations. Mean total bypass flows of $2.1 \pm 0.2 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ maintained mean arterial pressures in arch and descending aortic circulations of greater than 55 mm Hg. A mean differential of 4.3°C between arch and descending aortic temperatures was established before crossclamp application, and a mean maximum temperature differential of 7°C was established during bypass. A 2.4°C temperature differential was maintained at crossclamp removal. Cerebral and systemic venous oxygen saturation remained greater than 65% during bypass.

Conclusions: The Cobra device met all expectations for an arterial cannula with adequate perfusion to the arch and corporeal circulations. Dual perfusion with the Cobra catheter allows for independent temperature control during cardiopulmonary bypass with simultaneous cerebral hypothermia and systemic normothermia.

Neurologic complications of cardiac surgery are serious, frequent, and costly. Depending on the patient population, stroke might occur in 1% to 10% of patients,¹⁻³ with higher percentages experiencing encephalopathy or cognitive deficits. Sixty percent of patients undergoing coronary artery bypass grafting (CABG) might show cognitive deficits before hospital discharge. At 1-month follow-up, greater than 20% of these patients might remain unimproved.^{4,5}

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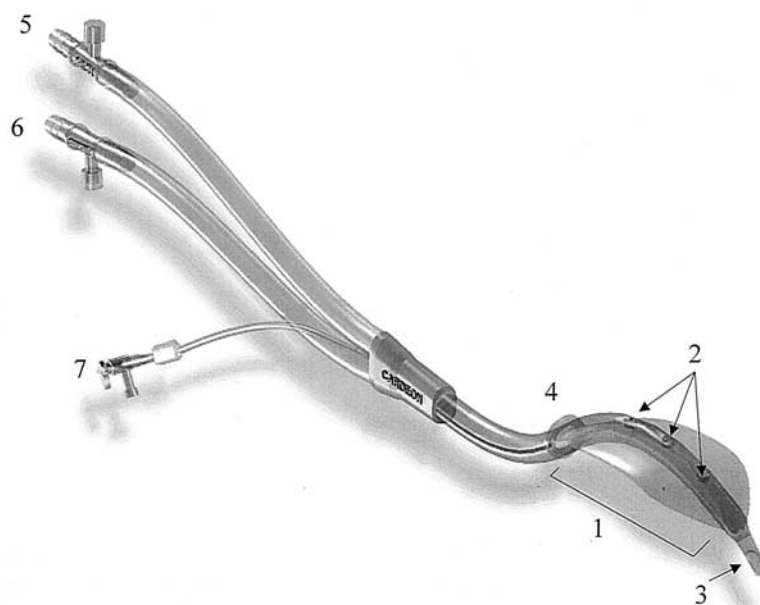


Figure 1. Schematic of the Cobra cannula demonstrating the baffle or wing (1), the arch perfusion ports (2), the descending aortic perfusion port (3), the sewing ring (4), 2 proximal connection ports (5 and 6), and the pilot balloon (7) for baffle inflation.

The ideal temperature for cardiopulmonary bypass (CPB) is a subject of debate. A body of evidence indicates that warm bypass can improve cardiac, pulmonary, and bleeding outcomes,⁶⁻⁹ but concerns about warm bypass persist^{10,11} because hypothermia is the most effective intervention for brain protection when ischemia occurs.^{12,13}

An optimal temperature-management strategy might combine cerebral hypothermia simultaneously with a warm body during CPB. A variety of interventions, including topical cooling and selective retrograde or antegrade perfusion, have been tried to provide more selective brain cooling during bypass.^{14,15} However, these techniques have not been embraced because they can be technically cumbersome. More recently, dual-temperature control through a single aortic catheter has been described.^{16,17}

In large-animal bypass studies the Cobra catheter (Cardeon Corp, Cupertino, Calif) has been shown to allow independent control of arch and descending aortic temperature.¹⁷ Additionally, it has been demonstrated to profoundly reduce brain and ocular embolization.¹⁸ These 2 features, intended to improve patient outcomes by regionalizing perfusion, have been termed *targeted circulatory management*. The aim of this investigation was to determine whether the Cobra catheter delivers adequate perfusion while providing cerebral hypothermia and relatively normothermic systemic temperature in adults undergoing CPB.

Methods

Patients from a general cardiac surgery population undergoing first-time elective surgery with CPB through a sternotomy were

eligible for participation. Enrollees were between 21 and 75 years of age, had a body surface area of 2.4 m² or less, and had both an ejection fraction and hematocrit level of greater than 30%. Patient exclusion criteria are provided in Appendix 1.

After institutional review board approval and written informed consent, final eligibility was determined with the intraoperative determination of aortic dimensions and severity of atherosclerosis. Grade IV atherosclerosis^{19,20} (severe; atheroma >5 mm in addition to ≥ 1 of the following: mobile or ulcerating lesions, extensive calcification, large protruding atheromatous debris or thrombus, or porcelain aorta) or an ascending aortic diameter of less than 19 mm or greater than 35 mm excluded patients intraoperatively before catheter placement.

The anesthetic management was according to the discretion of the attending anesthesiologist at each of the participating institutions. However, protocol required radial and femoral arterial lines, as well as a central venous pressure catheter or pulmonary artery catheter and transesophageal or epiaortic echocardiography for all patients. All patients had a No. 16 catheter placed retrograde into the jugular bulb through the internal jugular vein for intermittent sampling of cerebral venous oxygen saturation (SjVO₂). Patients had body temperature measured at both the bladder (descending aortic circulation) and the nasopharynx (n = 18), jugular bulb (n = 19), or both (arch circulation).

The CPB circuit selection was determined by the participating institutions; however, the circuit modification required for dual-temperature control was standardized. The primary heat exchanger was, as usual, incorporated into the hollow-fiber oxygenator. Distal to the oxygenator, a bifurcation in the tubing allowed the warm oxygenated blood to be delivered either to the catheter port supplying the distal lumen (descending aorta) of the Cobra catheter (Figure 1) or to a second heat exchanger (BIOtherm; Medtronic,

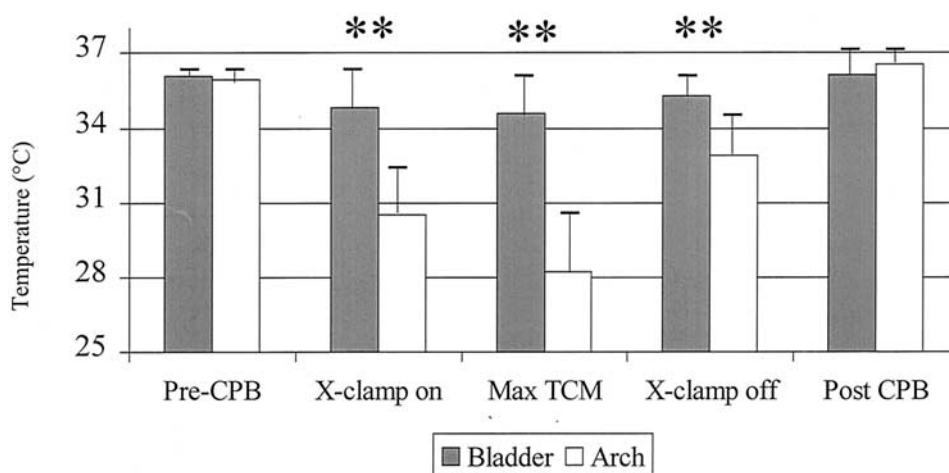


Figure 2. Bladder and arch (jugular bulb-nasopharyngeal) circulation temperatures during 5 study time points. Values shown are means \pm SD. **** $P < .001$** between 2 sites by paired t test ($n = 20$). *X-clamp*, Crossclamp; *TCM*, targeted circulatory management.

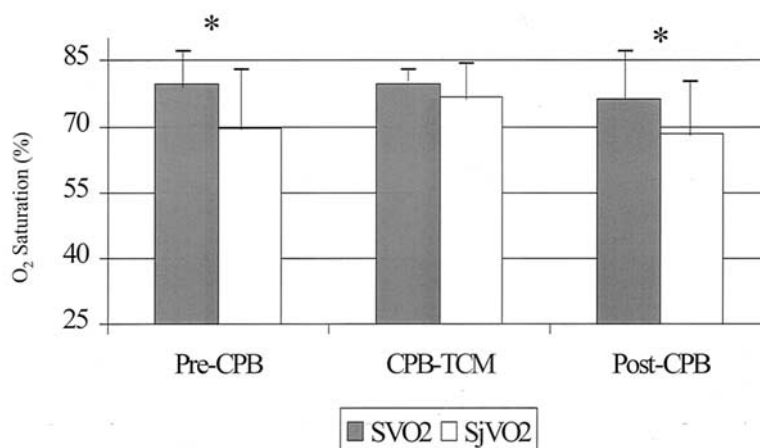


Figure 3. Jugular bulb ($SjVO_2$) and systemic mixed (SVO_2) venous oxygen saturations during 3 study time periods. Values shown are means \pm SD. *** $P < .01$** between the 2 circulations by paired t test ($n = 20$). *TCM*, Targeted circulatory management.

Minneapolis, Minn) used to cool the aortic arch perfusate. The hypothermic aortic arch perfusate was delivered to the proximal (arch) ports of the aortic catheter. An arterial filter (Affinity 351, Medtronic) was placed in both limbs of the aortic inflow line.

The Cobra catheter (Figure 1) is a 24F catheter and comes in 2 wing sizes (28 and 36 mm wing width). Catheter size selection and wing inflation volume were determined on the basis of descending aortic size. An aortic diameter of greater than 25 mm (measured echocardiographically 1-2 cm distal to the origin of the left subclavian artery) was the indication for the 36-mm wing. Wing inflation volume was determined with a nomogram on the basis of wing size and descending aortic diameter (Appendix 2).

After sternotomy and anticoagulation, the Cobra catheter was placed through a standard purse-string suture in the ascending aorta. Positioning was confirmed echocardiographically, and the 2

ports on the catheter were connected to the respective 1/4-inch (arch) and 3/8-inch (descending aortic) inflow lines. Venous cannulation was then completed, and CPB was initiated.

When CPB was established, the Cobra baffle or wing was inflated with saline, and cooling of the arch perfusate was initiated. An efficacy end point was to achieve 3°C of arch cooling measured at the nasopharynx or jugular bulb before placement of the aortic crossclamp. After crossclamp placement, the target temperature for the arch circulation was 28°C to 31°C. For the descending aortic circulation, the target temperature was 35°C to 37°C. The goal was to establish a minimum of a 5°C temperature gradient between the 2 circulations.

Temperatures, flows, and mean arterial pressures in arch (radial arterial line) and descending aortic circulations (femoral arterial line) were measured continuously, while venous blood samples

from the jugular bulb and bypass venous return line were drawn intermittently. The Cobra device used was rated for maximum flow rates of 2.75 L/min for the arch lumen and 3.25 L/min for the corporeal lumen, with a maximum pressure decrease of 200 mm Hg.

Patients were statistically characterized by using tables, figures, and descriptive statistics for demographic and baseline clinical variables. All statistical summaries and analyses were provided for the intent-to-treat population, which was defined as all consenting subjects who met the selection criteria. The one patient enrolled who did not undergo targeted circulatory management is included in the analysis of all data.

The analysis of variance technique was used to analyze the continuous variables, such as temperature, over time. A χ^2 test was used to analyze discrete variables, such as sex. Paired *t* tests were used to compare physiologic variables, such as venous oxygen saturation and temperature, in arch and descending aortic circulations.

Unless otherwise indicated, all comparisons of the treatment effect were performed with a 1-sided test at a less than .05 level of significance.

Results

Twenty patients at 3 institutions were enrolled between November 2000 and February 2001. The mean patient age was 62 ± 9 years. The mean weight and body surface area were 95 ± 16 kg and 2.1 ± 0.2 m², respectively. The mean preoperative ejection fraction was $57\% \pm 10\%$. Patients underwent isolated CABG (*n* = 13), valve (*n* = 3), and combined valve-CABG (*n* = 4) surgery with CPB by using the Cobra aortic catheter.

In 19 of the 20 patients, the Cobra catheter was successfully placed, requiring no repositioning. In one instance, after initial placement, initiation of cooling resulted in decreasing bladder temperature and a stable nasopharyngeal temperature. This temperature pattern did not change after rotation of the catheter by the attending surgeon, and therefore bypass proceeded with the use of the Cobra device as a standard aortic cannula (a single temperature was delivered through both perfusion lumens). In the remaining patients the Cobra catheter allowed for the rapid establishment of cerebral hypothermia relative to systemic normothermia.

Before bypass, mean arch (*n* = 20) and bladder (*n* = 19) temperatures were $35.9^\circ\text{C} \pm 0.5^\circ\text{C}$ and $36.1^\circ\text{C} \pm 0.3^\circ\text{C}$, respectively. With the onset of wing inflation and cooling, the arch perfusate temperature was initially set at a mean of 24.9°C , with the descending aortic perfusate temperature set at a mean of 35.3°C . The crossclamp was applied a mean of 3.4 minutes later, by which time a mean temperature differential between bladder and arch circulation of 4.3°C was established. The mean temperatures at this time were $30.5^\circ\text{C} \pm 2.1^\circ\text{C}$ at the nasopharynx or jugular bulb and $34.8^\circ\text{C} \pm 1.7^\circ\text{C}$ at the bladder.

In the 19 patients undergoing differential temperature management, the targeted maximum differential was

$6.7^\circ\text{C} \pm 0.8^\circ\text{C}$. A mean maximum temperature gradient of $7^\circ\text{C} \pm 1.2^\circ\text{C}$ was established at 22.0 ± 18 minutes of cooling time (Figure 2). At that time, mean arch and bladder temperatures were $28.2^\circ\text{C} \pm 2.2^\circ\text{C}$ and $34.6^\circ\text{C} \pm 1.7^\circ\text{C}$, respectively. Gradual rewarming of the arch circulation was initiated at the discretion of the surgeon, such that a modest temperature differential and mild cerebral hypothermia remained at the time of crossclamp removal. At crossclamp removal, temperatures in the arch and descending aortic circulations were $32.9^\circ\text{C} \pm 1.7^\circ\text{C}$ and $35.3^\circ\text{C} \pm 0.8^\circ\text{C}$, respectively. At that time, active rewarming of the arch circulation was stopped. During bypass with the Cobra device, all measured arch temperatures were lower than bladder temperatures, with a *P* value of less than .000 by using the paired *t* test. After weaning from bypass, the mean arch and bladder temperatures were $36.1^\circ\text{C} \pm 1.2^\circ\text{C}$ and $36.5^\circ\text{C} \pm 0.8^\circ\text{C}$ (Figure 2).

The mean duration of CPB and crossclamp time were 73 ± 21 and 49 ± 13 minutes, respectively. Mean total bypass flow with the Cobra device was 4.4 ± 0.5 L/min (2.1 ± 0.2 L · min⁻¹ · m⁻²), with mean flows to the aortic arch and descending aorta of 2.0 ± 0.4 and 2.5 ± 0.5 L/min, (0.9 ± 0.2 and 1.2 ± 0.2 L · min⁻¹ · m⁻²), respectively. These flows maintained mean arterial pressures in both circulations within the desired range (mean >55 mm Hg).

The adequacy of cerebral and systemic perfusion was assessed on the basis of measurements of mixed systemic venous oxygen saturation (SVO₂) and SjVO₂. Figure 3 shows the values for SVO₂ and SjVO₂ in the prebypass period during stable targeted circulatory management with the Cobra device and in the postbypass period. During stable CPB, the SVO₂ and SjVO₂ ranged from 71% to 87% and 68% to 98%, respectively. Before and after bypass, the SjVO₂ was lower than the SVO₂ (*P* = .004 and .003, respectively, paired *t* test), whereas during bypass, the 2 saturations did not differ.

Discussion

In the last 10 years, 2 practice issues receiving considerable attention in the cardiac surgical literature have been temperature management and cerebral embolization during CPB. With regard to temperature in cardiac surgical patients, there appear to be clear cardiopulmonary advantages to warm bypass. At the same time, the experimental literature indicates that hypothermia is the single best means to minimize the effects of cerebral ischemia. The last decade has also brought appropriate emphasis to the problem of cerebral embolization as a primary cause of brain injury during cardiac surgery. The Cobra aortic catheter, clinically described for the first time here, has been developed as the direct result of both of these discussions.

The Cobra device is unique in several ways. It is a dual-lumen aortic catheter intended as a substitute for a traditional aortic cannula and is capable of establishing and

maintaining cerebral hypothermia with simultaneous warm bypass to the rest of the body.¹⁷ By means of a second heat exchanger, we show that it is possible to establish greater than 3°C of cerebral hypothermia before crossclamp application and maintain cerebral hypothermia ($32.9^{\circ}\text{C} \pm 1.7^{\circ}\text{C}$) late in bypass at the time of crossclamp removal. This is important because aortic manipulation with the crossclamp is probably the most important cause of brain embolization in cardiac surgery.²¹⁻²⁵

In addition to providing brain cooling at the time of crossclamp placement and removal, a greater degree of cerebral hypothermia can be achieved and maintained through the bulk of the surgical procedure when using the Cobra catheter. In this study of 20 patients at 3 institutions, we achieved a maximum mean gradient of 7°C with a mean brain temperature of 28.2°C when the mean bladder temperature was 34.6°C. Greater degrees of cerebral hypothermia could be established in cases of longer duration without the requirement to cool the body to the same degree. Although not the design of this study, a brain temperature of 17°C to 20°C and a body temperature of 25°C to 27°C might be practical for such cases, reducing cooling, rewarming, and bypass time and potentially reducing the bleeding associated with profound whole-body hypothermia.

The other unique feature related to temperature management with the Cobra device is elimination of most of the need for rewarming. When this catheter is used, the bulk of body mass stays relatively normothermic. The requirement to replace the thermal debt is minimal, and therefore little energy needs to be applied to reach target temperature before weaning. This eliminates the overheating of the brain and cerebral oxygenation stress that can frequently occur when rewarming the body from hypothermic bypass.^{26,27} With the Cobra device, a low level of selective cerebral cooling can be maintained through the last part of bypass, or the temperature of the arch circulation can be gradually equilibrated with body temperature. Because high brain temperatures and low oxygen saturations during late bypass are associated with worsened neurologic outcome,²⁸ managing temperature in this fashion probably has cerebral advantages.

Although dual-temperature control expands what is possible during bypass and would be predicted to offer both neurologic and cardiac advantages, the Cobra catheter has a more unique feature that might prove more valuable than dual-temperature bypass.

A novel design feature of the Cobra catheter is a deployable wing that facilitates aortic arch flow segmentation and dual-temperature management. However, a more unique feature of this wing design is its ability to protect the cerebral circulation from embolization originating in the heart or aortic root.¹⁸ The catheter has a perfusion lumen on the cephalad surface of the cannula, as well as a distal port

that perfuses the descending aorta. The catheter is nonocclusive proximally, and the intrinsic resistance of the device results in a flow to the arch lumen that is high relative to the body surface area perfused. This results in continuous overflow around the proximal edge of the wing. This proximal overflow continually irrigates the aortic root and directs the blood in the root around the lesser curvature of the arch and down the descending aorta. In large-animal bypass studies the Cobra wing reduced embolization to the brain by approximately 90%.¹⁸ This dramatic result was achieved in the absence of any cerebral hypothermia. If cerebral cooling was added, we would predict that the reduction in brain embolization with the Cobra device would be even greater.

The Cobra device is easy to use and is equivalent in function to traditional arterial cannula with or without the use of the wing. The wing is prepared and deployed by using standard techniques (ie, fluid inflation with syringe). The catheter is placed through a standard ascending aortic aortotomy and is sized and shaped so that it sits in the middle of the flow stream in the transverse aortic arch. Its positioning is easily confirmed by imaging the distal portion of the cannula with transesophageal echocardiography. Perfusion with the device at conventional flow rates ($2\text{--}2.4 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$) results in mean arterial pressures above the autoregulatory threshold. The adequacy of cerebral perfusion and systemic perfusion is evidenced in this clinical trial by SjVO_2 and SVO_2 values equal to or greater than those seen under nonbypass conditions (Figure 3).

In one patient in this trial, use of the catheter resulted in temperature changes opposite those expected. Body temperature cooled, while the nasopharyngeal temperature remained warm. Rotation of the device did not change this situation, and therefore the surgeon elected to use the catheter as a conventional device. In retrospect, it is not possible to definitively determine the cause of the difficulty in this early case experience. It is possible that the catheter was rotated on insertion, such that the arch ports faced the lesser curvature of the aorta; however, rotation did not change the temperature control. It is more likely, however, that either the water lines to the arch and body heat exchangers or the connections for the 2 temperature probes were reversed. It should also be noted that this case was the first use of the Cobra device at that hospital. In greater than 130 subsequent clinical placements of the Cobra catheter at 15 institutions, this experience has not been repeated.

An experimental large-animal study has indicated that the Cobra device can dramatically reduce brain embolization by shunting those emboli down the descending aorta.¹⁸ It must therefore be asked whether use of this device would adversely affect organs supplied by the descending aorta. Although this trial is not designed to answer that question, we would speculate that this effect should be quite small. Both experimental¹⁸ and clinical²² studies found that the

mean percentage of the aortic embolic load entering the cerebral circulation was approximately 7% to 8%.^{18,22} As such, redirecting 90% of that 8% would have a small effect on the total embolization down the descending aorta. Furthermore, that additional fraction of emboli would be distributed to a much larger mass of body, and therefore the concentration effect of the redirected emboli should be very small. Additionally, those redirected emboli would be delivered to organs with much lower metabolic demands and better collateralization than the brain. Nevertheless, the randomized clinical outcome trial for the Cobra catheter will need to assess renal and visceral organ outcomes, as well as its neurologic effect.

In this investigation we demonstrate that the Cobra device meets the standards of adequacy of perfusion during bypass, as well as its ability to provide targeted dual-temperature control. Although this catheter is designed to provide neuroprotection by means of cerebral hypothermia and emboli reduction, it was not the purpose of this investigation to determine whether this device could improve neurologic outcome. Although 19 of the 20 patients in this trial underwent National Institutes of Health Stroke Scale assessment within 36 hours of operation and no patient demonstrated stroke or focal neurologic event, the study is not powered to provide neurologic outcomes. In contrast to this small prospective study, a neuroprotection trial must be randomized and appropriately powered for low-incidence events. A randomized, prospective, multicenter trial examining neurologic, cognitive, cardiac, pulmonary, and renal outcomes with the Cobra catheter has been initiated.

References

- Roach GW, Kanchuger M, Mangano CM, Newman M, Nussmeier N, Wolman R, et al. Adverse cerebral outcomes after coronary bypass surgery. Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation Investigators. *N Engl J Med*. 1996;335:1857-63.
- Tuman KJ, McCarthy RJ, Najafi H, Ivankovich AD. Differential effects of advanced age on neurologic and cardiac risks of coronary artery operations. *J Thorac Cardiovasc Surg*. 1992;104:1510-7.
- Wolman RL, Nussmeier NA, Aggarwal A, Kanchuger MS, Roach GW, Newman MF, et al. Cerebral injury after cardiac surgery: identification of a group of extraordinary risk. The Multicenter Study of Perioperative Ischemia (McSPI) Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. *Stroke*. 1999;30:514-22.
- Newman MF, Kirchner JL, Phillips-Bute B, Gaver V, Grocott H, Jones RH, et al. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. *N Engl J Med*. 2001;344:395-402.
- van Dijk D, Keizer AM, Diephuis JC, Durand C, Vos LJ, Hijman R. Neurocognitive dysfunction after coronary artery bypass surgery: a systematic review. *J Thorac Cardiovasc Surg*. 2000;120:632-9.
- Anonymous. Randomised trial of normothermic versus hypothermic coronary bypass surgery. The Warm Heart Investigators. *Lancet*. 1994;343:559-63.
- Birdi I, Regragui I, Izzat MB, Bryan AJ, Angelini GD. Influence of normothermic systemic perfusion during coronary artery bypass operations: a randomized prospective study. *J Thorac Cardiovasc Surg*. 1997;114:475-81.
- Flack JE 3rd, Hafer J, Engelman RM, Rousou JA, Deaton DW, Pekow P, et al. Effect of normothermic blood cardioplegia on postoperative conduction abnormalities and supraventricular arrhythmias. *Circulation*. 1992;86(suppl 5):II385-92.
- Yau TM, Carson S, Weisel RD, Ivanov J, Sun Z, Yu R, et al. The effect of warm heart surgery on postoperative bleeding. *J Thorac Cardiovasc Surg*. 1992;103:1155-63.
- Martin TD, Craver JM, Gott JP, Weintraub WS, Ramsay J, Mora CT, et al. Prospective, randomized trial of retrograde warm blood cardioplegia: myocardial benefit and neurologic threat. *Ann Thorac Surg*. 1994;57:298-304.
- Craver JM, Bufkin BL, Weintraub WS, Guyton RA. Neurologic events after coronary bypass grafting: further observations with warm cardioplegia. *Ann Thorac Surg*. 1995;59:1429-34.
- Ginsberg MD, Sternau LL, Globus MY, Dietrich WD, Busto R. Therapeutic modulation of brain temperature: relevance to ischemic brain injury. *Cerebrovasc Brain Metab Rev*. 1992;4:189-225.
- Busto R, Dietrich WD, Globus MY, Valdes I, Scheinberg P, Ginsberg MD. Small differences in intraschemic brain temperature critically determine the extent of ischemic neuronal injury. *J Cereb Blood Flow Metab*. 1987;7:729-38.
- Lytle BW, McCarthy PM, Meaney KM, Stewart RW, Cosgrove DM 3rd. Systemic hypothermia and circulatory arrest combined with arterial perfusion of the superior vena cava: effective intraoperative cerebral protection. *J Thorac Cardiovasc Surg*. 1995;109:738-43.
- Juvonen T, Zhang N, Wolfe D, Weisz DJ, Bodian CA, Shiang HH, et al. Retrograde cerebral perfusion enhances cerebral protection during prolonged hypothermic circulatory arrest: a study in a chronic porcine model. *Ann Thorac Surg*. 1998;66:38-50.
- Boston US, Sungurtekin H, McGregor CG, Macoviak JA, Cook DJ. Differential perfusion: a new technique for isolated brain cooling during cardiopulmonary bypass. *Ann Thorac Surg*. 2000;69:1346-50.
- Slater JM, Orszulak TA, Zehr KJ, Cook DJ. Use of the Cobra catheter for targeted temperature management during cardiopulmonary bypass in swine. *J Thorac Cardiovasc Surg*. 2002;123:936-42.
- Cook D, Zehr KJ, Orszulak TA, Slater JM. Profound reduction in brain embolization using an endoaortic baffle during bypass in swine. *Ann Thorac Surg*. 2002;73:198-202.
- Mills NL, Everson CT. Atherosclerosis of the ascending aorta and coronary artery bypass: pathology, clinical correlates, and operative management. *J Thorac Cardiovasc Surg*. 1991;102:546-53.
- Montgomery DH, Ververis JJ, McGorisk G, Frohwein S, Martin RP, Taylor VR. Natural history of severe atheromatous disease of the thoracic aorta: a transesophageal echocardiographic study. *J Am Coll Cardiol*. 1996;27:95-101.
- Blauth CI, Cosgrove DM, Webb BW, Ratliff NB, Boylan M, Piedmonte MR, et al. Atheroembolism from the ascending aorta: an emerging problem in cardiac surgery. *J Thorac Cardiovasc Surg*. 1992;103:1104-12.
- Barbut D, Yao FS, Lo YW, Silverman R, Hager DN, Trifiletti RR, et al. Determination of size of aortic emboli and embolic load during coronary artery bypass grafting. *Ann Thorac Surg*. 1997;63:1262-7.
- Pugsley W, Klinger L, Paschalis C, Treasure T, Harrison M, Newman S. The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. *Stroke*. 1994;25:1393-9.
- Fearn SJ, Pole R, Wesnes K, Faragher EB, Hooper TL, McCollum CN. Cerebral injury during cardiopulmonary bypass: emboli impair memory. *J Thorac Cardiovasc Surg*. 2001;121:1150-60.
- Borger MA, Ivanov J, Weisel RD, Rao V, Peniston CM. Stroke during coronary bypass surgery: principal role of cerebral macroemboli. *Eur J Cardiothorac Surg*. 2001;19:627-32.
- Cook DJ, Oliver WC Jr, Orszulak TA, Daly RC. A prospective, randomized comparison of cerebral venous oxygen saturation during normothermic and hypothermic cardiopulmonary bypass. *J Thorac Cardiovasc Surg*. 1994;107:1020-9.
- Cook DJ, Orszulak TA, Daly RC, Buda DA. Cerebral hyperthermia during cardiopulmonary bypass in adults. *J Thorac Cardiovasc Surg*. 1996;111:268-9.
- Croughwell ND, Newman MF, Blumenthal JA, White WD, Lewis JB, Frasco PE, et al. Jugular bulb saturation and cognitive dysfunction after cardiopulmonary bypass. *Ann Thorac Surg*. 1994;58:1702-8.

Appendix 1

Patient exclusion criteria

1. Patient with a myocardial infarction (<1 week)
2. Patient requires inotropic agents (eg, vasoconstrictive-vasodilatory) or mechanical support (eg, intra-aortic balloon pump)
3. Positive pregnancy test result
4. Patient is currently in atrial fibrillation
5. Patient has a history of severe chronic obstructive pulmonary disease, chronic bronchitis, and emphysema; is extubated; has uncontrolled asthma or forced expiratory volume in 1 second value of less than 70% of predicted value or documented pneumonia; or has other severe pulmonary disease within the month of admission
6. Patient has a history of severe hypotension (systolic blood pressure < 70 mm Hg within 1 week of surgical intervention)
7. Patient has a history of cerebrovascular disease (cerebrovascular accident-stroke, reversible ischemic neurologic deficit, or transient ischemic attack); previous carotid artery intervention or significant (>50%) carotid stenosis, as determined by means of ultrasonic Duplex scanning; symptomatic head trauma; seizures; or other neurologic disorder
8. Patient's left radial artery is being harvested for CABG
9. Patient has a history of severe peripheral vascular disease (history of diminished or absent femoral pulses, hip claudication, deep venous thrombosis, systolic blood pressure difference of > 15 mm Hg between the left and right arms)
10. Patient has a history of hepatic disease (aspartate aminotransferase level \geq 50 U/mL, bilirubin level > 1.5 mg/dL, or increased prothrombin time of > 5 seconds above control values), bleeding disorder, or coagulopathy
11. Patient has received short-acting IIb/IIIa medications (eg, eptifibatide [Integrelin]) in the last 8 hours or long-acting IIb/IIIa medications (eg, abciximab [ReoPro]) in the past 24 hours
12. Patient has renal insufficiency during this hospitalization (creatinine level > 2.5 mg/dL and blood urea nitrogen level > 50 mg/dL)
13. Patient has severe systemic disease (eg, lupus, heart failure, cold agglutinin syndrome, terminal cancer, pancreatic biliary disease, and/or uncontrolled diabetes)
14. Patient has calcification of aorta on routine preoperative angiography, if available, or aortic aneurysm
15. Patient has uncontrolled hypertension (blood pressure > 185/95 mm Hg on antihypertensive medications)
16. Patient has score of less than 20 on Folstein Mini Status Examination
17. Patient is currently participating in another device-drug trial
18. Patient has any other significant medical factor that in the judgment of the physician would exclude the patient from participating

Appendix 2. Wing size and inflation volumes on the basis of aortic diameter

Aorta size	Cobra wing size	
	28 mm	36 mm
19-20 mm	6 mL	
21-22 mm	7 mL	
23-24 mm	7 mL	
25 mm	7 mL	
26-28 mm		12 mL
29-32 mm		12 mL
33-35 mm		12 mL